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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/655,547
Filing Date: September 04, 2003
Appellant(s): ROBERTS ET AL.

Roberts et al.

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/12/2006 appealing from the Office action mailed 1/9/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims: appealing from the Office Action mailed on 1/9/2006.

Claim Rejections - 35 USC § 112

Written Description

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 182-196 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 182-196 are drawn to a method for detecting pregnancy in a bovine animal. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

"[A] generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." (emphasis added)

The court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product (emphasis added).

Thus, the instant specification may provide an adequate written description of the species, such as PAG4, 6, 7, 16, 17, 20, 21, per Lily by structurally describing a representative number of PAGs that are capable of being an early pregnancy detector of bovine and become undetectable about 2 months post-partum, or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe all the PAGs required to practice the method of claim 182 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any PAG, nor does the specification provide any physical or chemical characteristics of the other PAGs nor any *functional characteristics coupled with a known or disclosed correlation between structure and function* (emphasis added).

The specification describes only a few PAGs where structural diversities exist among the different PAGs, ranging from 50% to 90% homology (See Figure 4 in both protein and nucleic acid identity comparison). With such diversity in terms of both amino acid and nucleic compositions among the few representatives (boPAG 1 to boPAG 12), one ordinary skill in the art would not conclude that applicant sufficiently describe a "representative number" of such species (note, boPAG1 is not within the recited PAGs since it can be detected at about two month of post-partum). In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." As indicated by the case law that "[a] definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." 43 USPQ2d at 1405. It is noted that applicant describes some sequence identity around the

catalytic aspartic acid residues (Asp 32 and Asp 215) among some BoPAGs, including boPAG 1-12 (See Figure 1). However, there is no further study correlating this region to the asserted function, i.e. present early in pregnancy and undetectable at about two months post-partum, using site-directed mutagenesis to ascertain the structural contribution to this functionality. Thus the specification does not provide an adequate written by merely reciting the function limitations of the PAGs, such as detectable in early pregnancy and undetectable at 2-month post-partum.

(10) Response to Argument

(A) The rejections of claims 182-196 are alleged improper under 35 USC 112, first paragraph, as failing to comply with the Written Description requirement.

(1) Applicant alleges that the specification describes PAGs supporting the full claim scope.

Applicant argues that examiner's assertion with respect to show complete structure of any PAG is erroneous because seven PAGs have been provided and disclosed in the specification. Thus, applicant has satisfied written description requirement under 35 USC 112, first paragraph, in supporting the full claim scope.

Applicant arguments have been considered, but are not persuasive.

As indicated in the *Final Office* Action under this issue (See page 7, Section A)-

"[I]t is not mainly *the number, i.e. how many PAGs, is disclosed in the specification. It rests also in the correlation of structure and functionality. Examiner pointed out that the specification does not provide sufficient analysis or data establishing or corroborating such correlation, therefore the specification fails to support the full scope of claims."*

The essential material issue here is whether these seven PAGs are sufficient to convey the information to one ordinary skill in the art that the applicant has in fact invented the subject matter which is claimed. Therefore, the applicant is entitled to the protection of what he actually possesses. (See In re Barker "The purpose of written description requirement is to ensure that the scope of the right to exclude....does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification" 559 F.2d 588 (CCPA 1977)). Examiner considers seven PAGs are not sufficient to satisfy the full claim scope not mainly is the number per se, but also want of correlation with respect to the functionality (See below discussion).

(2) Applicant alleges that the PAGs disclosed are representative of the claim scope.

Applicant argues that it is not required by case law (*Eli Lilly*) to provide every species encompassed by the invention. Applicant argues that no basis or number, if necessary satisfied the genus of PAGs with recited functional feature, e.g. present in early pregnancy and undetectable at about two months post-partum, were ever clearly set forth by the examiner. Applicant concludes that the structure of the seven PAGs disclosed in the specification satisfied "representative number" standard set forth under Lilly decision.

Applicant arguments have been considered, but are not persuasive.

As indicated in the Final Office Action (page 8, Section B)-

"[I]t is not mainly the number of the species constituting the full scope of the claim, namely genus. It also needs corroborating evidence, i.e. correlation of functionality and structure, sufficiently to one ordinary skill in the art to conclude applicant possess the whole genus. Second, examiner acknowledges the diversity of structures among the PAGs, however examiner points out that the conserved regions among diversity does not amount to justification of possessing the whole genus without further correlation study.

The main issue is not how many PAGs would be sufficient to constitute a "representative" of the scope for the genus. Rather the main concern is whether these seven PAGs are sufficient to provide information with respect to the *correlation* of functionality and structure to one ordinary skill in the art (emphasis added). It is true that the *Eli Lilly* court does not hold that every species encompassed by a genus need to be specifically described; however the court further indicates that

"[A] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, *which feature constitute a substantial portion of the genus"* (Id, at 1569).

There is no correlation provided in the specification with respect to relationship between the structures and the functionality of PAGs. Applicant merely compared different PAGs with respect to the homology of amino acid (See Figure 1). For example specification at page 61, line 4-10, applicant states-

"A considerable degree of amino acid sequence identity exists among the 12 boPAGs listed in FIG. 1. The most related are boPAG1 and boPAG3, sharing a 86% amino acid identity. The least related are boPAG4 and boPAG10 with only 49% identity. Interestingly boPAG1 and boPAG4, which as noted above cross-react with the anti-boPAG1 antiserum, exhibit only 76% identity at the amino acid level. Presumably a common epitope exists on the two molecules."

The sequence comparison results show some degree of identity, e.g. 86% (note, boPAG1 is not within the recited PAGs since it can be detected at about two month of post-partum). There is no teachings or discussion about which portion or fragment of the PAGs contributes for the recited function. Particularly, the identity map in Figure 1 and Figure 2 merely show random homology among the PAGs. The results of the comparison, at most, show some degree of identity among the PAG, yet merely disclosure of the seven PAGs sequence and sequence comparison, is not sufficient to justify for occupying the whole genus.

(C) Applicant asserts the disclosure is commensurate with the claims.

Applicant argues that examiner misunderstood the meaning of "functionality" of PAGs, and the working examples and figures disclosed in the specification describe a correlation of structure (sequence and comparison) and functionality (appropriately temporally defined expression in appropriate tissue) that allow one skill in the art to identify PAGs.

Applicant arguments have been considered, but are not persuasive.

First of all, it appears to the examiner that applicant now introduces a new feature not recited in the claim, namely "appropriately temporally defined expression in appropriate tissue" as defined for the term "functionality" (See above). The recited claim language for the functionality is that the selected PAGs antigen in the sample that is "present early in pregnancy and is undetectable at about two months post-partum, whereby detection of said PAG indicates the animal is pregnant" (See claim 182). The assertion is not consistent with the claim language. Second, the instant invention is to detect samples from "saliva, serum, blood, milk or urine" of the suspected bovine animal. These are biological fluid samples. Whereas the so-called temporally control is from solid tissue, i.e. placenta. At page 66, line 22 to page 67, line 6, applicant states as follows:

Results: The length of gestation in cattle is about 285 days. Initial immunoscreening of cDNA libraries previously identified three boPAG (boPAG1, 2 and 3). More recently two additional cDNA (boPAG13 and boPAG14) were cloned from mRNa of term placenta by using hybridization screening (SEQ ID NO: 13) and (SEQ ID NO:14) in a day 260 placental cDNA library (Xie et al, 1991; Xie et al., 1995). On day 25 pregnancy, ten distant PAG were identified (Example 1, FIG. 1, FIG. 2 and FIG. 5). Only boPAG2 was isolated from both stages of pregnancy. These cloning data imply that expression of individual boPAG is **temporally controlled**. To confirm the temporal expression of boPAG, ribonuclease protection assays were carried out to delineate the stages at which individual boPAGgenes were expressed in the **cattle placenta**. This procedure was repeated at least twice for each boPAG riboprobe and for each RNA sample. The major band represents the protected boPAG mRNA. In addition, there were multiple small bands in each lane. Those smaller

bands almost certainly protected sequences highly related to, but distinct from, that of the riboprobe"

The term of "temporal" appears only in the above section in the specification. No teachings disclosed or suggested such "temporal control" correlate with the early present of PAGs and disappearance at about two months post-partum. Therefore applicant's arguments are not material to the claim language

Applicant further asserts that the conserved regions of PAGs would allow identification of members of this claimed genus to function as early markers for detection of pregnancy in bovine. Since these PAGs are naturally occurring proteins in the bovine placenta, therefore, "*their function was studied, as disclosed in the specification, by assessing the temporal pattern of their expression and their subsequent presence in appropriate tissue*" (See Brief page 5, last paragraph to first paragraph of page 6). Applicant provides evidence of example 2 (conservation analysis) and Example 3-4 (functional analysis) in support of this argument. With respect to BoPAG1, applicant asserts that this antigen is not within the scope of the claimed method.

Applicant arguments have been considered, but are not persuasive.

As discussed before that the instant invention is to detect biological fluid samples, e.g. serum, milk, or urine, not the solid tissue such as placenta during pregnancy (Example 3-4). Additionally, applicant has not established any correlation between the PAGs in the fluid samples versus the placenta tissue. Thus the assertion is not pertinent. With regarding to BoPAG1, examiner acknowledges that this antigen is not within the scope of the claimed method. Therefore, the example of using BoPAG1 should be withdrawn.

Applicant argues that the specification describes a number of physical or chemical characteristics of PAGs (See e.g. Abstract, specification page 19-26, Examples 1-3). Applicant argues that based on the "*shared identity at the amino acid level, and, importantly, are expressed in appropriate tissues and in an appropriate temporal*

manner, present early in pregnancy and undetectable at about two months post-partum, such that they may be identified as BoPAGs that could be useful in the claimed methods for early detection of pregnancy in bovine animals." (See Brief page 6, third paragraph). Applicant further argues the disclosure of specification satisfied under *Enzo* decision in that "*by disclosure of sufficiently detailed, relevant identifying characteristics....i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics*" (296 F. 3d at 1324). Applicant further argues that Figure 4 provides evidence of substantial identity among bovine PAGs at both nucleic acid and amino acid level. Such conservation is further illustrated in the sequence alignments provided in Figure 1 and as phylogenic tree shown in Figure 5. These evidence indicates that the PAGs have conserved regions and share a common ancestry. Thus the PAGs detected in the claimed method share both structural and functional characteristics (See Brief, page 8, second paragraph).

Applicant arguments have been considered, but are not persuasive.

To the contrary, the examiner's rebuttal is not inconsistent with the holdings of *Enzo*. As set forth in the *Enzo*, the court requires one ordinary skill to demonstrate "functional characteristics when coupled with a known or disclosed *correlation* between function and structure" of the claimed subject matter (emphasis added). As discussed before, applicant has not provided sufficient evidence justifying of possession of the genus because no correlation of the structure of such genus with the characterized function was disclosed. Examiner acknowledges the experimental data of structural analysis of the PAGs. However, there is no evidence disclosed in the specification indicating which region or segment conserved and correlating to the recited functions. For example, Figure 4 as emphasized by applicant, shows "*substantial identity* among bovine PAGs at both nucleic acid and amino acid level" (page 7, last paragraph). Nevertheless, the comparison of various PAGs at both DNA and amino acid levels merely shows homology of different PAGs, ranging from 49% to 91%. No study has shown what particular region(s)

contributes to the claimed function. Similarly Figure 1 and 2 also present amino acid sequence comparison among different PAGs. Still, no data indicate any particular region contributing to the claimed characteristic function.

Applicant argues that the genus of PAGs is limited because such PAGs are naturally produced by bovine animals, and the sequences have been shown to be related. The biology of the animal thus dictates a finite and limited class of PAGs. Furthermore, one ordinary skill in the art can utilize molecular techniques based on the homology information to screen placenta tissues to further isolate novel PAGs that are present early in pregnancy and are undetectable at about two months post-partum.

Applicant arguments have been considered, but are not persuasive.

With respect to the limitedness of the natural occurring PAGs, the assertion still cannot remedy the deficiency of the functional correlation requirement as set forth under *Enzo*. Furthermore, if the number is limited and sequenced/identified, applicant is entitled of protection to all the *identified* PAGs. With respect to the further isolate and identify PAGs using molecular techniques, the specification does not indicate what distinguishing attributes shared by PAGs other than simple homology analysis. No common structure attributes identify the members of the genus, particular to the correlation of the claimed function. The present data in the specification were merely an invitation to further experiment but not sufficient to convey the message to one artisan in the field that applicant possesses of the genus because a patent is not a hunting license, it is not a reward for the search, but compensation for its successful conclusion. See Adang v. Fishhoff, 286 F.3d 1346 (Fed. Cir. 2002).

(B) Applicant asserts that claims 182-196 satisfy the Enablement Requirement under 35 USC 112, first paragraph.

Examiner considers the arguments persuasive because it would not impose undue experimentation to one ordinary skill in the art to screen, isolate and identify the PAGs for the purported function to detect early pregnancy in the bovine animal. Note, applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is *severable* from its enablement provision (See 19USPQ2d 1111, 1115)(emphasis added).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Jacob Cheu

Art Unit 1641

August 24, 2006

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